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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,792	02/05/1999	ALDO T. IACONO	P32130	4164

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EXAMINER
TRAVERS, RUSSELL S

ART UNIT	PAPER NUMBER
1617	

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23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/244,792	Applicant(s) Iacono
	Examiner R.S. Travers J.D., Ph.D.	Art Unit 1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 19-48 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 19-48 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The request for reconsideration filed May 3, 2003 has been received and entered into the file.

Applicant's arguments filed May 3, 2003 have been fully considered but they are not deemed to be persuasive.

Claims 19-48 are presented for examination.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 19-48 are rejected under 35 U.S.C. § 103 as being unpatentable over Adjei et al and Waldrep et al, in view of Gilbert et al, Knight et al and Applicant's admission on the record.

Adjei et al, Waldrep et al, Gilbert et al, Knight et al and Applicant admits on the record the claimed compounds as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form. These medicaments are

taught as useful for treating graft rejection, inflammation and those conditions herein claimed and disclosed. Claims 22, 23, 24, 27, 29, 33, 34, 42 and 45, and the primary references, differ as to:

1) recitation of various un-encapsulated dosage forms, and,

2) dosage levels herein claimed.

Attention is directed to Adjei et al, Waldrep et al, Gilbert et al and Knight et al teaching the various encapsulated, and organic solvent aerosol formulations as an improvement over simple aerosol employment of the powdered active ingredient. Examiner cited prior art teaches powdered cyclosporine as useful for an anti-inflammation, and anti-rejection medicament administered by aerosol. The skilled artisan would have possessed all conventional administration regimens, and seen the selection of one or another as the simple selection from among obvious alternatives. In the instant case, this selection process need not be reached. Adjei et al, Waldrep et al, Gilbert et al and Knight et al teach cyclosporine as useful by aerosol administration, as herein claimed. It is noted that Adjei et al, Waldrep et al, Gilbert et al and Knight et al recite the use of unencapsulated cyclosporine administered by aerosol inhalation; although this method is not claimed.

Determining the active ingredient dosage level required to effect optimal therapeutic benefit is well within the Skilled Artisan's purview and the benefits of achieving such maximization obvious, to said skilled artisan. Attention is directed to

Adjei et al (column 8) teaching the normal practice of dosage maximization by the attending medical professional. The claims merely recite the obvious employment of old and well known active ingredients, carriers and excipients. Thus, the only issue presented in the instant application is the obviousness of the claimed compositions and therapeutic methods.

Claim 47 specifically requires a pharmaceutical composition wherein the particle size is 0.1-2.0 microns. Adjei et al teach particle sizes encompassing this claimed range.

Claim 43 requires propylene glycol carrier or excipient to administer the active ingredients. This carrier is taught as old and well known by Waldrep et al (see column 4, line 59).

Attention is directed to claims reading on cyclosporine powder, at a particular size range, absent carriers or excipients. Such claims read on the compounds herein disclosed, and taught as old by the Examiner cited prior art.

RESPONSE TO ARGUMENTS

Examiner finds those rebuttal arguments presented in paper 22 unconvincing. Those rejections set forth by Examiner in papers 4, 8, 14 and 20 rest on a firm factual and legal foundation. Attention is directed to Gilbert et al experimenting with small particle aerosol cyclosporine administration, teaching encapsulated cyclosporine "as effective as free CsA (cyclosporine A). Examiner notes this passage from Gilbert et

all would suggest Applicant's statements suggesting a failure by the cited prior art to teach un-encapsulated cyclosporine are not factually based. Simply stated, if those cyclosporine dosages administered neat are therapeutically superior to more involved administration methods, a showing of such unexpected benefits are in order.

As previously stated, is well known by the skilled artisan that carriers and excipients are employed to enhance the activity of active ingredients. Thus, the skilled artisan would expect conventional excipients and carriers to be useful concomitantly, absent information to the contrary. The instant carriers and excipients are not employed concomitantly in the prior art, thus only obviate their concomitant use.

Applicants constructively aver unexpected benefits residing in the claimed subject matter, yet fail to fails to set forth evidence substantiating this belief. Evidence as to unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). Applicants have not provided data illustrating unexpected benefits residing in the recited subject matter reasonably commensurate in scope with the instant claims. Absent claims commensurate with a showing of unexpected benefits, or a showing reasonably commensurate with the instant claims, such claims remain properly rejected under 35 USC 103.

As stated previously, and above, Adjei et al, Waldrep et al, Gilbert et al and Knight et al teach encapsulation as an improvement over simple powder aerosol administration; making statements to these facts. Additionally, Examiner takes notice of phosphatidylcholine as an "organic solvent". Waldrep et al also teach Applicants' organic solvent as useful for the instant claimed utility. If the medicament is old and well known for the use herein claimed, Applicant has the burden to illustrate the instant claimed invention possesses those benefits absent the additional carriers or excipients. Examiner notes the cited prior art teaches incomplete encapsulation of the claimed medicament, although failing to teach an effective dosage of these medicaments.

As stated above, Adjei et al, Waldrep et al, Gilbert et al and Knight et al teach encapsulated cyclosporine as an improved aerosol delivery system. Examiner cited prior art also teaches the optimal particle size and requisite dosage. In the instant case, Applicant is attempting to recapture the state of the art superseded by Adjei et al, Waldrep et al, Gilbert et al and Knight et al.

Applicants aver unexpected benefits residing in the claimed subject matter, yet fail to fails to set forth evidence substantiating this belief. Evidence as to unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). Applicants have not provided data illustrating unexpected benefits residing in the recited subject matter reasonably

commensurate in scope with the instant claims. Absent claims commensurate with a showing of unexpected benefits, or a showing reasonably commensurate with the instant claims, such claims remain properly rejected under 35 USC 103.

It is well known by the skilled artisan that carriers and excipients are employed to enhance the activity of active ingredients. Thus, the skilled artisan would expect conventional excipients and carriers to be useful concomitantly, absent information to the contrary. The instant carriers and excipients are not employed concomitantly in the prior art, thus only obviate their concomitant use.

Applicant's attention is drawn to In re Graf, 145 USPQ 197 (CCPA 1965) and In re Finsterwalder, 168 USPQ 530 (CCPA 1971) where the court ruled that when a substance is unpatentable under 35 USC 103, it is immaterial that applicant may have disclosed an obvious or unobvious further purpose or advantage for the substance.

Examiner would favorably consider claims directed to those medicaments providing unexpected therapeutic benefits, as averred herein.

Examiner cited prior art teaches the claimed compounds alone, or with simple carriers as useful for treating those graft rejections herein claimed. Failure to claim such simple and fundamental medicament administration procedures fail to diminish those teachings. Additionally, Applicant appears to be arguing a much more limited invention than herein claimed; rebuttal arguments based on unclaimed limitations are moot. If medicament application produces an expected therapeutic outcome, that

therapeutic outcome is anticipated; regardless the recitation of that inherent therapeutic benefit.

The instant claims are directed to employing an organic solvent, a very broad carrier recitation for such a crowded field. A simple oil, or those ingredients employed for encapsulation, would meet an "organic solvent" limitation.

As stated above, the discovery of a mechanism by which a drug is taken up by a biological system fails to distinguish over the same administration system before such discoveries.

Applicant's claims administered in an "organic solvent" read on any organic carrier, such as liposomes, or dry powder carried by air. Attention is directed to Waldrep et al teaching dry particle cyclosporine administration (see column 1), or "organic solvents" (ethanol, or propylene glycol). Applicant's presented claims are extremely broad, thus, are easily met by the Examiner cited prior art. Those inventions argued appear to be much more limited than those claims presented. Examiner can not read limitations from the specification into the presented claims. Only limitations specifically recited in the presented claims will serve to distance the envisioned invention from the cited prior art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). The practice of automatically extending the

shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Russell Travers at telephone number (703) 308-4603.

Russell Travers J.D., Ph.D.
Primary Examiner
Art Unit 1617